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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,103	09/09/2003	Daikichi Fukushima	Q77131	3399

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

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10/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/657,103	FUKUSHIMA ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/700,397.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11 September 2007 has been entered.

Status of Application, Amendments and/or Claims

The amendment of 11 September 2007 has been entered in full. Claims 1 and 10 are amended. Claims 2-9 are cancelled.

Claims 1, 10, and 11 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejections of claims 1 and 10 under 35 U.S.C. § 112, first paragraph (scope of enablement and written description) for recitation of polypeptide variants as set forth at pages 10-14 of the previous Office Action (12 February 2007) are *withdrawn* in view of the amended claims (11 September 2007).

2. The rejection of claims 1, 2, and 10 under 35 U.S.C. § 112, first paragraph (new matter) as set forth at pages 14-15 of the previous Office Action (12 February 2007) is *withdrawn* in view of the amended and cancelled claims (11 September 2007).

3. The rejections of claims 1, 2, and 10 under 35 U.S.C. 112, second paragraph, as set forth at pages 15-16 of the previous Office Action (12 February 2007) are *withdrawn* in view of the amended claims and cancelled claims (11 September 2007).

Claim Rejections - 35 USC § 101 and 35 U.S.C. § 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 10, and 11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth at pages 3-9 of the previous Office Action and at pages 5-8 of the Office Action of 07 June 2006.

The claims are directed to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 3. The claims recite a composition containing the polypeptide in association with pharmaceutically acceptable diluent or carrier. The claims also recite a polypeptide comprising the amino acid sequence of SEQ ID NO: 4.

Applicant's arguments in the response submitted 11 September 2007 as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant argues that OC001 is identical to human neurotrimin. Applicant has attached alignments between OC001 (SEQ ID NOs: 3, 4) and human neurotrimin. Applicant concludes that OC001 is human neurotrimin. Applicant asserts that OC001 causes neurite outgrowth.

Applicant states that the specification discloses that OC001 shares activities with the nervous cell adhesion molecule family including rat neurotrimin and OBCAM. Applicant submits that since OC001 is 70% and 91% homologous to rat neurotrimin and OBCAM, one of ordinary skill in the art would appreciate that OC001 shares neurotrimin and OBCAM properties based on homology alone.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed in the previous Office Action of 12 February 2007, the specification of the instant application teaches that a search using BLASTX, BLASTP, and FASTA revealed a significant homology between clone OC001 and rat neurotrimin (Genbank Accession No. U16845) and OBCAM (Genbank Accession No. L34774) (page 28, first full paragraph). The specification also discloses that "[b]ased on these homologies, clone OC001 and nervous cell adhesion molecule family including neurotrimin and opioid-binding cell adhesion molecule were expected to share at least some activity" (page 28, lines 22-25). However, as pointed in the previous Office Actions of 12 February 2007 and 07 June 2006, while it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. The assertion that the disclosed OC001 polypeptide has biological activities similar to known neurotrimin and OBCAM cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of polypeptide families wherein individual

members have distinct, and sometimes even opposite, biological activities (see for example, Tischer et al. (U.S. Patent 5,194,596);; Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596;; Vukicevic et al. (1996, PNAS USA 93:9021-9026);; Massague (1987, Cell 49:437-8, esp. p. 438, column 1, second full paragraph to the end);; Pilbeam et al. (1993, Bone 14:717-720); see p. 717, second paragraph of Introduction;; Kopchick et al. (U.S. Patent 5,350,836)).

Additionally, the specification at pages 14-22, discloses an extensive list of many diverse biological activities that the OC001 polypeptide may exhibit (such as, cytokine activity, cell proliferation/differentiation activity, immune stimulating/suppressing activity, hematopoiesis regulating activity, tissue generation/regeneration activity, among others). Within this list, the specification of the instant application teaches that "[t]he present polypeptide is also suspected to function to nervous system, so expected to have functions below....spread of neural dendrites..." (pg 22, lines 1-5). However, it is not even clear from the teachings of the specification if the polypeptide is intended to *inhibit or promote* spread of neural dendrites. The specification does not clearly teach that OC001 causes neurite outgrowth, as asserted by Applicant. Furthermore within nine pages of potential activities the claimed polypeptide may have, Applicant has now purportedly identified that OC001 causes neurite outgrowth. Thus, it is clear from the instant specification that a specific and substantial utility for OC001 was not disclosed in the specification or well known in the art as of the effective filing date of the present application. Utility is determined as of the effective filing date of the application (See *In re Brana*, 51 F.3d at 1567 n.19, 34 USPQ2d at 1441 n.19). The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement in the context of a claim to DNA. See *In re Fisher*, 421

F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The Fisher court interpreted *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966), as rejecting a "de minimis view of utility." 421 F.3d at 1370, 76 USPQ2d at 1229. The Fisher court held that § 101 requires a utility that is both substantial and specific (1371, 76 USPQ2d at 1229). The court held that disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." (76 USPQ2d at 1230). The court held that a specific utility is "a use which is not so vague as to be meaningless." In other words, "in addition to providing a 'substantial' utility, an asserted use must show that that claimed invention can be used to provide a well- defined and particular benefit to the public." Regarding the instant application, the claimed OC001 polypeptide is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

(ii) Applicant indicates that as of the filing date, Pimenta et al. disclosed that neurotrimin and OBCAM, together with LAMP and GP55, were IgLON family members. Applicant argues that Gil et al. and Wilson et al. acknowledged that receptors belonging to the IgLON family induce neurite outgrowth via homophilic interactions with neuronal cells. Applicant states that the same reference discloses that inhibition occurs, via heterophilic interactions with neuronal cells,

potentially, in the absence of the receptor. Applicant indicates that Gil et al. disclose that neurotrimin induces neurite outgrowth in DRG neurons whereas neurotrimin inhibits outgrowth in SRG neurons, and that said properties are comparable to homophilic interactions with DRG neurons in which neurotrimin is expressed and to heterophilic interactions with SRG neurons in which neurotrimin is not expressed. Applicant adds that Wilson et al. disclose that *GP55* inhibits the neurite outgrowth of DRG neurons. Applicant argues that Gil et al. disclose GP55 is not expressed in the DRG neurons used by Wilson et al. and thus would induce the neurite outgrowth in older DRG neurons in which GP55 is expressed. Applicant concludes that since the dual aspect of OC001 is based on a recipient and not on OC001 proper, OC001 regulates neurite outgrowth of neuronal cells vis-à-vis the recipient.

Applicant's argument has been fully considered but is not found to be persuasive. The Examiner acknowledges that the state of the art is such that IgLON family members (such as neurotrimin and OBCAM) are expressed on distinct populations of neurons and have opposing activities on different types of neurons (i.e., inhibit one group of neurons while enhancing another). However, it is important to note that the specification of the instant application does not teach which cells express the claimed OC001 polypeptide. Gil et al. even conclude that studies suggest "...that the distinct expression of IgLON members promotes the development of system-specific projections by a combination of growth-promoting and growth-inhibiting activities. The precise signaling pathways involved and the functional consequences of interactions between different family members are important questions for future investigation" (bottom of pg 9323 through the top of pg 9324).

(ii) Applicant asserts that the reference of McNamee, published in 2002 does not reflect the appropriate state of the art. Applicant has concluded that only McNamee et al. allege that any receptor belonging to the IgLON family does not relate to neurite outgrowth.

Applicant's argument has been fully considered but is not found to be persuasive. Specifically, the post-filing date reference of McNamee et al. was cited by the Examiner in the previous Office Action to emphasize that as of 2002, there was inconclusive evidence for a role of IgLON members in neurite outgrowth. At page 941 and page 947, McNamee et al. review other studies with IgLON family members and the differing functions of each. At the top of page 942, column 1, McNamee et al. state that the ability of OBCAM (which Applicant asserts OC001 has homology to) to modify neurite outgrowth has not yet been studied. McNamee et al. also disclose that IgLONs are thought to either enhance or inhibit neurite outgrowth (page 942, top of column 1). McNamee et al. also disclose that their current study failed to find conclusive evidence for a role of IgLON members in neurite outgrowth or axon guidance (abstract; pg 947, col 2, 1st full paragraph). Thus, in view of the state of the art as cited by McNamee et al. as well as the post-filing date observations of McNamee et al., one skilled in the art would not know the functional activity of the purported IgLON family member, OC001. For example, the skilled artisan would not know which neuron population OC001 exerts its activity on or even what the precise biological activity is (i.e., stimulation or inhibition of neurites, cell adhesion, or other).

It is noted that it is not clear how Applicant has concluded that only McNamee et al. allege that any receptor belonging to the IgLON family does not relate to neurite outgrowth. Applicant did not cite a specific passage from McNamee for support.

5. Claims 1, 10, and 11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at page 9 of the previous Office Action (12 February 2007) and at page 8 of the Office Action of 07 June 2006.

Applicant states that a specific, substantial, and credible utility has been described above. Specifically, since Applicant has not provided evidence to demonstrate that the OC001 polypeptide has a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention. It is noted that the instant specification is required to teach one skilled in the art how to make and use the OC001 polypeptide.

Conclusion

No claims are allowable.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
26 October 2007

Bridget E. Bunner

BRIDGET E. BUNNER
PRIMARY EXAMINER